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ORIGINAL ARTICLE

SILENT MYOCARDIAL ISCHEMIA IN TYPE 2 DIABETIC PATIENTS WITH MICROALBUMINURIA

Hasan Akbar Khan[1&2], Muhammad Shuaib[3], Saman Sabir[4], Ayesha Aimen[5], Murtaza Bukhari[6], Muhammad Irfan[7]

[1]Department of Biochemistry, Al-Aleem Medical College, Lahore, [2]Institute of Molecular Biology and Biotechnology, The University of Lahore, Departments of [3]Medicine & [7]Pediatric Medicine, Mohiuddin Teaching Hospital, Mirpur, AJK, [4]Department of Biochemistry and Molecular Biology, University of Gujrat, Gujrat, Punjab, [5]Department of Pediatric Medicine, CMH Kharian, Kharian Cantt, Punjab, [6]Department of Medicine, Hayat Memorial Teaching Hospital Continental Medical College, Lahore, Punjab, Pakistan

ABSTRACT

Background: Silent myocardial ischemia (SMI) is more prevalent in type 2 diabetes mellitus (T2DM) patients, resulting in worse cardiovascular outcomes in the future. Therefore, it's early and prompt diagnosis is the need of the hour. It can be identified by traditional cardiac stress testing such as exercise tolerance test. Presence of SMI can also be predicted by microalbuminuria as it can significantly forecast any future cardiovascular event. The objective of this study was to find out the frequency of SMI in T2DM patients with microalbuminuria.

Materials & Methods: A cross-sectional survey was carried out at the Diabetes Research Centre Outpatients Clinic, Nishtar Hospital, Multan, 01/01/2020 to 30/06/2020. After taking informed consent, patients having T2DM and microalbuminuria were included. Every participant had to undergo exercise tolerance test (ETT). Patients were regarded as having SMI if they fulfilled Bruce protocol and had myocardial ischemia on stress ETT. All gathered data was analyzed using SPSS version 24. Mean and standard deviation was measured for age and duration of DM. Frequency and percentage was measured for gender and presence or absence of SMI as confirmed by ETT.

Results: This study comprised of a total 81 patients. Mean age of patients was 49.72±6.75 years, with range of 30. Male patients were 49(60.5%) whereas 32(39.5%) were female. Mean duration of T2DM was 12.52±4.71 years. SMI was present in 34 (41.9%) T2DM patients with microalbuminuria, as confirmed by ETT. Among the positive cases, majority belonged to 51-60 years age group (50.0%) and most of them were males 20 (58.8%). The majority of patients aged more than 60 years had SMI (85.7%), detected by ETT.

Conclusion: Frequency of SMI in the current study (41.9%) is startling and direct us for earlier diagnosis and management of T2DM and microalbuminuria to prevent any cardiovascular event. Screening with ETT should be done for SMI in every diabetic patient with microalbuminuria.

KEY WORDS: Type 2 Diabetes Mellitus; Microalbuminuria; Silent Myocardial Ischemia; Exercise tolerance test.

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1. INTRODUCTION

Type 2 Diabetes mellitus (T2DM) is termed as an inability to form or respond to insulin, resulting in impaired carbohydrates, protein, and fat metabolism and an increased plasma glucose levels.[1] It is a major public health issue, accounting for approximately 536.6 million cases all over the world. It is estimated to be increasing to 783.2 million by the year 2045.[2] The significant part of this rise will take place in developing countries like Pakistan.[3] The prevalence of DM has significantly increased in Pakistan. In the year 2021, approximately 33 million adult population had DM in Pakistan-a 70% rise since 2019.[4] Cardiovascular disease (CVD) is a significant medical and public health concern all around the world. T2DM is a recognized predisposing factor of CVD. In addition, T2DM patients with myocardial ischemia have worse cardiovascular outcomes and relatively increased in-hospital morbidity and mortality rates.[5] Silent myocardial ischemia (SMI) is prevalent in T2DM patients

Corresponding Author:

Dr. Muhammad Shuaib
Associate Professor
Department of Medicine
Mohiuddin Teaching Hospital, Mirpur, AJ&K
E-mail: drshuaibm@yahoo.com

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and may hamper or conceal the detection of ischemic heart disease, especially in its initial phase. The prevalence of SMI among patients having T2DM is high, ranging from approximately 20% to more than 50%.[6] SMI can be detected by various tests including coronary angiography, CT angiography, thallium scan, stress echocardiography, and exercise tolerance test (ETT). SMI is termed as stress-induced ST-segment depression on ECG without presence of any other symptoms of CVD.[7]

Diabetic nephropathy (DN) is one of the most prevalent causative factors of end-stage renal disease (ESRD) all over the world, causing significant morbidity and mortality.[8] Microalbuminuria, excretion of 30-300 mg albumin per day in urine, takes place before the nephropathy appears & it serves as a marker of prediction for higher morbidity and mortality due to CVD.[9] Prevalence of microalbuminuria in type 2 DM is 31.56% in Pakistan.[10] In a recent study including type 2 DM patients, 16(29.6%) patients were having SMI among 54 patients with microalbuminuria [11].

Rationale of the present study was to find out the frequency of SMI in T2DM patients with microalbuminuria. It is of great importance because accessibility and affordability of health care services is not adequate in the local population as compared to other populations so the delay is anticipated in early diagnosis of DM and SMA. It will ultimately help in reducing the associated morbidity and mortality because very scarce literature demonstrating the role of microalbuminuria in type 2 DM patients regarding SMI development is available in the local settings.

2. MATERIAL AND METHODS

A cross-sectional study was brought off at Diabetes Research Centre Outpatients Clinic, Nishtar Hospital, Multan, form 01/01/2020 to 30/06/2020. Sample size was estimated using prevalence of SMI in T2DM patients as 30% [12,] margin of error as 10%, and level of significance as 95%. It turned out to be 81. Purposive sampling technique was utilized to draw the sample. Study comprised of 81 T2DM patients having microalbuminuria, regardless of age, gender, time span of T2DM and use of anti-diabetic medication. Patients having congestive heart failure, uncontrolled hyperglycemia, fever, urinary tract infection, and pregnancy were not included in the study.

A detailed questionnaire was designed to collect data. Prior permission was acquired from the ethical committee of the institution. Informed consent was also obtained from every study participant. Any patient visiting the OPD of Diabetes Research center Nishtar Hospital Multan is registered only when he or she gets following investigations done: fasting or random blood sugar, Hemoglobin A1c, electrocardiography, urinary albumin level, Fasting Lipid Profile, and Anti-HCV. Once a patient was found to have microalbuminuria, he/she underwent exercise tolerance test (ETT) utilizing Bruce protocol.[13] Baseline twelve lead ECG was done before initiation of test. All gathered data was analyzed using SPSS version 24. Mean and standard deviation was measured for age and duration of DM. Frequency and percentage was measured for gender and presence or absence of SMI as confirmed by ETT.

3. RESULTS

Study comprised of a total 81 patients. Table 1 demonstrates the baseline characteristics of study participants. Mean age of patients was 49.72±6.75 years, with range of 30. 49(60.5%) patients were male whereas 32(39.5%) were female. 8.6% patients belonged to 31-40 years age group, 48.1% to 41-50 years age group, 34.6% to 51-60 years age group and 8.6% to age group 61-70 years. Among 81 patients, mean duration of T2DM was 12.52±4.71 years. SMI, confirmed by ETT, was present in 34 (41.9%) T2DM patients with microalbuminuria, as illustrated in figure 1.

Table 1: Baseline characteristics of the patients (n=81)

Characteristics	Frequency	Percentage
Gender of study participants		
Male	49	60.5
Female	32	39.5
Age of study participants* (years)	49.73±6.75	
31-40	7	8.6
41-50	39	48.1
51-60	28	34.6
61-70	7	8.6
Duration of DM* (years)	12.51±0.52	

N = Number of study participants; DM = diabetes mellitus; * = mean ± standard deviation was used to demonstrate the data.

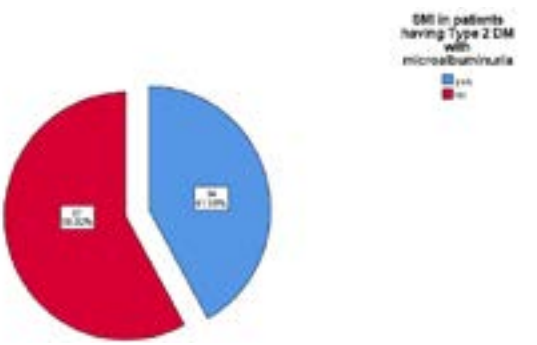

Figure 1: Silent myocardial ischemia in patients having type 2 diabetes mellitus with microalbuminuria, confirmed by exercise tolerance test

Table 2 comprises of age and gender distribution of ETT results demonstrating SMI in microalbuminuria positive diabetic patients**.** Among the positive cases, majority belonged to 51-60 years age group (50.0%) and most of them were males 20 (58.8%). Majority of the patients aged more than 60 years had SMI (85.7%), detected by ETT.

Table 2: Age and gender distribution of ETT results in microalbuminuria positive diabetic patients (n=81).

Parameters	Positive N (%)	Negative N (%)
Age groups (years)		
31-40	1 (2.9)	6 (12.8)
41-50	10 (29.4)	29 (61.7)
51-60	17 (50.0)	11 (23.4)
61-70	6 (17.6)	1 (2.1)
Gender		
Male	20 (58.8)	29 (61.7)
Female	14 (41.2)	18 (38.3)

ETT = Exercise tolerance test; N= number of study participants; % = percentage of study participants.

4. DISCUSSION

Diabetes mellitus is a serious public health problem causing various adverse events. Number of patients suffering from DM is increasing all around the world with every passing year.[14] Individuals with T2DM have a higher likelihood of developing morbidity and mortality, particularly from CVD, than the non-diabetic individuals.[15] T2DM enhances the risk of developing cerebrovascular, coronary, and peripheral arterial diseases up to 4 times, in addition to causing kidney, lungs, pancreas, gut, and eye diseases.[16] Recently, a number of studies have proposed microalbuminuria as a potent predisposing factor of causing cardiovascular in type 2 diabetic patients[17,18], in addition to the conventional predisposing factors such as hypertension, hyperlipidemia, obesity, and smoking.[19] Patients with microalbuminuria have 8-15 fold higher risk of cardiovascular mortality than those without microalbuminuria.[8] However, there is very scarce local literature available on this topic. Persistent microalbuminuria has been linked to cause a higher chance of developing coronary atherosclerosis and cardiovascular events leading to increased number of deaths. Hence, regular screening ought to be done for microalbuminuria in patients with T2DM.[20] Although, SMI usually occurs in T2DM, yet it is more prevalent in T2DM with microalbuminuria.[6] Thus, microalbuminuria may be utilized as a premature predictor and a predisposing factor of CVD.[17] Individuals with positive ETT are at 10 fold increased probability of having symptomatic disease in future as compared to individuals with negative findings.[21]

The present study, including 81 diabetic patients with microalbuminuria, was carried out at Diabetes Research Centre Outpatients Clinic, Nishtar Hospital, Multan. It was designed to find out the frequency of SMI in T2DM patients having microalbuminuria and revealed that the frequency of SMI among patients with T2DM having microalbuminuria was 34 (41.98%), as confirmed by ETT. Although the frequency is fairly high, yet quite similar to frequencies reported by various studies conducted previously in different regions.[12,22]

In a study conducted by Hussain et al. it was found out that 23.8% patients of type 2 DM had microalbuminuria. Among them, 29.6% patients with microalbuminuria had silent myocardial infarction [12]. Rutter et al. demonstrated SMI in 65% of patients with microalbuminuria and 40% of patients with normoalbuminuria. This difference exists may be due to variation in the age and gender distribution in Rutter et al study. Also, majority was taken from diabetes centers situated in the region with higher reported prevalence of cardiovascular diseases. However, comparatively younger patients (49.73±6.75 years) with a close male-female ratio presented to a general hospital were included in the current study. Contrastingly, if patients aged more than 60 years were taken, the frequency of SMI would be much higher, depicting an increased prevalence of SMI in the older diabetics.[23]

A high percentage of 34.04% patients with microalbuminuria had evidence of SMI, in a study conducted by Chain et al., juxtaposed to 6.38% patients with normoalbuminuria ($P<0.05$).[7] In a study carried out by Russo et al. Microalbuminuria found to be more prevalent in diabetic CVD class juxtaposed to diabetic no CVD class (25.3% vs 19.2%).[24] Emami et al. demonstrated that SMI was found in 65% of all type 2 DM patients. Stress induced ischemia on myocardial perfusion imaging was evident in 87.5% of patients with microalbuminuria and in 39.3% patients with normoalbuminuria. Frequency of stress induced ischemia was 10.81 times more in patients with microalbuminuria ($p<0.001$).[25] Hussein et al. showed that the frequency of SMI in T2DM patients with microalbuminuria and normoalbuminuria was 30% and 6.6% respectively. It also showed that surprisingly with a maximal stress, MI may be totally masked in T2DM patients [12]. Chauhan et al. reported that type 2 DM patients with microalbuminuria have significant association with SMI, as evident by ETT ($p<0.001$).[3]

In a study conducted by Hafsa et al. it was revealed that SMI was found in 44.9% patients, identified by ETT.[26] Mean age of patients in that study was 49.92±5.55 years, comparable to those in the present study. There were 60.5% male and 39.5% female

patients in the current study. These findings are in accordance with the study of Hafsa et al.[26]

5. CONCLUSION

Frequency of SMI in the current study (41.9%) is startling and direct us for earlier diagnosis and management of T2DM and microalbuminuria to prevent any cardiovascular event. Screening with ETT should be done for SMI in every diabetic patient with microalbuminuria.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	HAK, MS
Acquisition, Analysis or Interpretation of Data:	HAK, MS, SS, AA, MB, MI
Manuscript Writing & Approval:	HAK, MS, SS, AA, MB, MI

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.